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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Marcus A. Horwitz	:	Group Art Unit 186
LEGIONELLOSIS VACCINES AND METHODS FOR THEIR PRODUCTION	:	Examiner: Mohamed, A.
Serial No. 232,664	:	
Filed: August 16, 1988	:	
	:	Docket No.: 70-155

DECLARATION UNDER RULE 132

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

I, Marcus A. Horwitz, M.D., declare and state that:

1. I am the inventor in the above-identified patent application.

2. I received my M. D. Degree from Columbia University College of Physicians and Surgeons, New York, New York in June of 1972 and am currently Professor of Medicine and of Microbiology and Immunology, Chief, Division of Infectious Diseases, Department of Medicine, UCLA School of Medicine, Center for the Health Sciences at Los Angeles, California. A copy of my current curriculum Vitae

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detailing my Education, Internship and Residency, Public Health Service Positions, Clinical Fellowships, Research Fellowships, Faculty Positions, Certifications, Affiliations, Honors and Awards, Scientific and Editorial Boards and Study Sections, Publications, Abstracts, and Presentations at National or International Meetings was previously made of record as Exhibit 1 to my earlier Declaration Under Rule 132 filed June 4, 1990. As indicated in my Curriculum Vitae, I have extensive experience in the fields of Microbiology, Immunology and Infectious Diseases.

3. I have reviewed the Official Action dated December 11, 1990, and have carefully studied the Examiner's statements therein.

4. I understand the Examiner has interpreted the disclosure of my invention as being enabling only for claims limited to the method of producing and using vaccine against Legionella pneumophila or Mycobacterium tuberculosis infections in guinea pigs. In contrast to this interpretation of my patent application, I believe that those skilled in the art will find the specification of my application to be sufficiently enabling to support a method for producing and using mammalian vaccines against specific intracellular pathogens that produce one or more extracellular products which in turn induce strong cell mediated immune responses (such as lymphocyte proliferative responses or cutaneous delayed type hypersensitivity responses) in mammalian hosts which are

infected with or immune to the specific intracellular pathogen of interest.

5. More specifically, in the study of protective immunity, particularly of protective immunity in humans, where an animal model has been available every vaccine ever developed was done so in the animal model which mimicked the disease condition in humans or the target species. This is standard procedure in this field of technology for reasons of safety and expense. Where appropriate animal models are available they are always used to study protective immunity in target species other than the laboratory model itself.

6. The success of utilizing laboratory animal models is predicated on the understanding that immunodominant epitopes frequently cross species. Thus, an immunodominant molecule in one species, for example a rodent or guinea pig, will very frequently be immunodominant in a different species such as in humans.

7. For example, guinea pigs are more susceptible to pulmonary tuberculosis than humans. Accordingly, the fact that my invention enables us to induce protective immunity in guinea pigs from lethal challenge with Mycobacterium tuberculosis is more significant than our ability to do so in humans which are less susceptible to tuberculosis. Moreover, the successful results in guinea pigs are readily extrapolated into successful results in humans or other

less susceptible mammals with similar disease patterns.

8. More importantly, my laboratory has been able to produce actual data with Mycobacterium tuberculosis extracellular protein showing that humans who have been infected previously with tuberculosis bacilli react to the extracellular proteins of Mycobacterium tuberculosis in an in vitro lymphocyte proliferation assay whereas control human subjects who have not been previously infected do not react with this extracellular protein.

9. Taken in conjunction with the previously submitted data regarding inducing protective immunity in guinea pigs, this result conclusively establishes the validity of the guinea pig laboratory model and its interspecies applicability as the extracellular protein of Mycrobaterium tuberculosis induces cell-mediated immunity in humans as well as in the standard guinea pig laboratory model.

10. In conclusion, where it possible for the Examiner to limit the scope of my disclosure to the laboratory model alone, it would be impossible to obtain meaningful patent coverage for any vaccine known to man. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine, or

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imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the above-identified patent application or any patent issuing thereon.

Date: 5/8/91

Marcus A. Horwitz, M.D.